

ABSTRACT

The present invention relates to the preparation of non-human animals having chimeric livers, whereby some or substantially all of the hepatocytes present are human hepatocytes. It is based, at least in part, on the discovery that rats, tolerized *in utero* against human hepatocytes, were found to serve as long-term hosts for human hepatocytes introduced post-natally, and the introduced hepatocytes maintained their differentiated phenotype, as evidenced by continued production of human albumin. The present invention further relates to the use of such animals as models of various liver diseases, including viral infection. Such embodiments are based on the discovery that transplanted human hepatocytes in chimeric livers were found to be susceptible to Hepatitis B virus and Hepatitis C virus infection.